AR/1632

PTO/SB/21 (09-04) MODIFIED IFW

TRANSMITTAL FORM

Application Number:	09/351,778
Filing Date:	July 12, 1999
First Named Inventor:	William S.M. Wold
Art Unit:	1632
Examiner Name:	Scott David Priebe
Total Number of Pages in this Submission : _____	**Attorney Docket Number:** INGN:109US

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  - ☐ Affidavits/declaration(s)
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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Wold *et al.*	Group Art Unit: 1632
Serial No.: 09/351,778	Examiner: Priebe, Scott David
Filed: July 12, 1999	Atty. Dkt. No.: INGN:109US
For: REPLICATION COMPETENT ANTI-CANCER VECTORS	

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David L. Parker

REQUEST FOR REHEARING UNDER 37 C.F.R. §41.52

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Commissioner:

In accordance with 37 C.F.R. §41.52, Appellants herein submit this Request for Rehearing. The Decision on Appeal was mailed on January 24, 2006. In accordance with 37 C.F.R. §41.52, the deadline for filing the Request for Rehearing is March 24, 2006. Therefore, this request is timely filed. No fees are believed due in connection with this submission. However, the Commissioner is authorized to deduct any fees that may become due under 37 C.F.R. §§ 1.16 to 1.21 from Fulbright & Jaworski, L.L.P. Account No. 50-1212/INGN:109US.

GROUNDS FOR REQUEST

A. PROCEDURAL HISTORY AND REQUEST FOR RELIEF

Regarding the above-referenced patent application, Appellants initially filed their appeal brief on July 26, 2004, in response to the final Office Action dated February 19, 2004. A Supplemental Appeal Brief in response to a Notice of Non-Compliance under 37 C.F.R. §1.192(c), dated September 9, 2004, was filed on November 3, 2004. An Examiner's Answer was mailed on December 29, 2004, and a Reply Brief in response to the Examiner's Answer was submitted on February 22, 2005. A Decision on Appeal was mailed on January 24, 2006. Appellants herein submit this Request for Rehearing in accordance with 37 C.F.R. §41.52.

This submission is specifically directed to three distinct rejections affirmed by the Board. Appellants request that the Board reconsider and reverse each of these rejection, or in the alternative, remand these rejections to the examiner for further development of the record with respect to evidentiary underpinnings of the rejections. Appellants failure to address any other grounds for rejection also affirmed by the Board in this Request is not intended as a waiver of Appellants rights with respect thereto. Indeed, Appellants may, subsequent to the Board's decision on this Request, seek relief by way of appeal to the Federal Circuit for any and all remaining issues.

B. SUMMARY OF ARGUMENT

In accordance with 37 C.F.R. §41.52, Appellants submit this Request for Rehearing to request that the Board of Patent Appeals and Interferences reconsider its Decision on Appeal dated January 26, 2006, and reverse the following rejections:

- the rejection of claims 11-13, 32-44, 60, 61, 68, 69, 72-75, 97-99, and 101-108

under 35 U.S.C. §102(e) as being anticipated by either Henderson or Little;

- the rejection of claims 13, 20-22, 60, and 64-66 under 35 U.S.C. §103(a) as being unpatentable over Henderson or Little as combined with Freytag; and
- the rejection of claims 32 and 104-106 under 35 U.S.C. §112, first paragraph.

With regard to these rejections, Appellants submit that the Board:

1) applied an inappropriate "inherency" analysis with regard to the §102(e) rejection of claim 13 and claims depending therefrom;

2) failed to conduct a proper analysis to determine whether the patents cited as art under §102(e) claim the same subject matter as do Appellants, thereby impacting the availability of Rule 131 declarations submitted during the prosecution below; and

3) failed to base its decision on enablement of claims 32 and 104-106 on substantial evidence. A detailed discussion of these issues is presented *infra*.

1. Standard of Review

The Federal Circuit has held that findings of fact by the Board of Patent Appeals and Interferences must be supported by "substantial evidence" within the record. *In re Gartside*, 203 F.3d 1305, 1315 (Fed. Cir. 2000). In *Gartside*, the Federal Circuit stated that "the 'substantial evidence' standard asks whether a reasonable fact finder could have arrived at the agency's decision." *Id.* at 1312. See also *Matsushita Elec. Indus. Co. v. United States*, 750 F.3d 927, 933 (Fed. Cir. 1984) (A decision is supported by substantial evidence when "a reasonable mind might accept [it] as adequate to support a conclusion."). Accordingly, it necessarily follows that an Examiner's position on appeal must be supported by "substantial evidence" within the record in order to be upheld by the Board of Patent Appeals and Interferences.

2. Substantial Evidence Supports a Reversal of the Rejections of Claims 11-13, 32-44, 60, 61, 68, 69, 72-75, 97-99 and 103-108 Under 35 U.S.C. §102(e) and §103(a) Over Henderson or Little[1]

a) The Board Failed to Establish a Proper Basis for its "Inherency" Rejection of Claims 11-13, 32-44, 103-106 and 108 Under §102(e) Over Henderson or Little

At page 14 of the Decision on Appeal, the Board provides its explanation as to why it believed the Henderson and Little references anticipated certain claims of the present application despite the absence of ***any*** discussion of overexpression of ADP. After mentioning the overexpression limitation found in Appellants' claim 13, the Board provides an inherent anticipation argument, concluding, we submit without a complete examination of the evidence, that the burden has been shifted to Appellants on this issue. The only evidence upon which the Board relied was the alleged similarity of methods by which the respective adenoviruses were made. The Board's opinion, however, apparently failed to consider the evidence on the ***face*** of Henderson/Little (raised by Appellants in their Brief at pages 19-20) that demonstrated that their construct ***did not*** overexpress ADP

Appellants first note that inherency rejections are only proper where there is ***certainty*** with regard to the subject matter of the reference. *MEHL/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999) (quoting *In re Oelrich*, 666 F.2d 578, 581 (CCPA 1981)). Thus, comments such as "absent evidence to the contrary" and "would expect" evince a misapplication of the inherency doctrine, and an attempted shifting of burdens without a sufficient evidentiary bases. Indeed, the Board's statement that "there is nothing on the record that demonstrates that the recombination ADP expressing adenoviruses of Henderson and Little do not meet [Appellants'] level of ADP expression" shows precisely the nature of the Board's

[1] Applicants do not seek to request rehearing of the rejections as they apply to claims 101 and 102.

error – it assumes that the mere ***possibility*** of anticipation is sufficient to support the rejection. However, the case law is crystal clear that far more is required.

In point of fact, the record contains far more conclusive evidence on this issue and demonstrates that the Henderson and Little adenoviruses did ***not*** overexpress ADP as compared to wild-type. Appeal brief at pages 15-16. To summarize, Henderson states that CN751 kills cells more efficiently than an ADP-minus control, ***but about the same as an ADP-positive wild-type control***, Rec700. Henderson, col. 49, lines 6-8; Little, col. 40, lines 24-26. Because cell killing is a good measure of ADP expression (see Example 2 of the present specification), it also is known that *dl309*, the standard against which claim 13 and claims depending therefrom are measured, expresses "wild-type" levels of ADP. Specification at page 25, lines 28-30. Since Henderson and Little state that CN751 expresses wild-type levels of ADP, it can be concluded that CN751 does not anticipate any claim requiring ***over***expression of ADP (*e.g.*, present claim 13). Thus, the only evidence of record on this point contradicts the Board's conclusion.

The Board erroneously dismissed this evidence and line of reasoning by stating that "the claim does not require any particular level of overexpression ...." Decision on Appeal at page 14. That statement is incorrect, and even the Board acknowledges this when it admits that the overexpression must be at least in excess of *dl309*, *Id.* Moreover, this level of overexpression, defined as at least in excess of wild-type, was specifically upheld by the Board as sufficiently supported by the specification in response to an enablement challenge. Decision on appeal at page 7. And finally, because Henderson and Little acknowledge that their vectors ***do not*** overexpress ADP as compared to wild-type, Appellants submit that there is no reason – explicit or inherent – to read their disclosures as providing the ADP ***overexpression*** recitation of the rejected claims. So, the Board is incorrect both in arguing (a) that there is not a valid basis for

comparing the presently claimed vectors with those of Henderson and Little, and (b) that there is insufficient evidence showing that Henderson and Little fail to provide vectors that meet the limitations of Appellants' claims. As such, Appellants maintain their position that the §102(e) rejections are not based on accurate factual or legal bases.

b) Substantial Evidence Does Not Support the Board's Holding that Appellants Must Make a Showing Under 37 C.F.R. §41.202

In its decision, the Board also refused to consider Rule 131 declarations submitted by Appellants showing invention of the claimed subject matter prior to the effective dates of the Little and Henderson references. In so doing, the Board found that because Little and Henderson ***claimed*** the same subject matter as Appellants, Rule 131 declarations were not proper. However, there is ***no*** evidence of record to support the Board's finding regarding the interfering nature of the appealed claims as compared to those of Henderson or Little, much less the substantial evidence required by *Gartside*.

In order for the Board's position to be proper, the appealed claims would need to be drawn to the same patentable subject matter as the claims of Henderson or Little, *i.e.*, to ***interfere*** with the claims of those references. In view of the current interference rules as well as controlling case law, the standard here is "two-way" patentability: "[a]n interference exists if the subject matter of a claim of one party would, if prior art, have anticipated or rendered obvious the subject matter of a claim of the opposing party **and *vice versa***." 37 C.F.R. §41.203(a) (emphasis added); *Winter v. Fujita*, 53 USPQ2d 1234, 1243 (BPAI 1999).

Anticipation, in this context, requires that a patent claim recite every limitation of the presently claimed invention, either explicitly or inherently. See *In re Schreiber*, 128 F.3d 1473, 44 USPQ2d 1429, 1432 (Fed. Cir. 1997). Further, to establish a *prima facie* case of obviousness, the claim must: (1) teach or suggest all the claim limitations; (2) provide some suggestion or

motivation to modify the reference; and (3) provide a reasonable expectation of success. MPEP §2142; *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed Cir. 1991). As will be explained below, the Board failed to make a proper showing on the issue of two-way anticipation or obviousness for the relevant claims.

The first mention of this issue is at page 16 of the Decision on Appeal, where the Board notes that Rule 131 declarations cannot be relied upon to overcome a patent reference where that reference claims the same invention. The only discussion of whether Appellants do, in fact, claim the same invention as Little and Henderson comes at pages 16-17 of the Decision on Appeal, where it is stated that "representative claim 13 is generic to Little's claim 63" and "representative claim 60 is also generic to Little's claim 63." While Appellants disagree,[2] this would at most establish ***one-way*** anticipation, which is not the standard for assessing the existence of interfering subject matter. As discussed above, in order for there to be conflicting subject matter, a ***two-way*** analysis of patentable distinction must be performed. Here, however, ***no*** analysis of ***patentable distinction*** was provided beyond that stated above. Thus, there is no substantial evidence of record upon which one could base a conclusion that Appellants are claiming the same invention as Henderson or Little.

In conclusion, in the absence of a rigorous comparison of the claims of Henderson and Little with those of the present application – a comparison based on evidence of record – the Board cannot shift the burden to Appellants to make the showing required by 37 C.F.R. §41.202 to provoke an interference. Therefore, it is respectfully submitted that the Board erred in failing to consider the Rule 131 declarations and address their impact on the rejections under 35 U.S.C. §102(e) and 35 U.S.C. §103(a) over Henderson and Little.

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[2] For example present claim 13 requires overexpression of ADP, which recitation is nowhere found in the ***claims*** of Henderson or Little. Similarly, representative claim 72 specifies a particular structure for the vector, namely, the absence of an E3 splice site, that also is missing from Henderson's and Little's claims.

c) *Substantial Evidence Supports a Finding that Appellants Are Not Claiming the Same Subject Matter as Henderson and Little*

Although not required to do so, Appellants provide the following explanation of why substantial evidence supports a finding that Appellants are ***not*** claiming the same invention as Henderson and Little.

(1) Comparison of Claim 63 of Little with Present Claims 13 and 60

Claim 63 of Little, cited in the Decision on Appeal, is represented below, in comparison with claims 13 and 60 of the present application, the independent claims. Points of commonality are shown with bold type, and underlining indicates points of distinction:

Claim 63 of Little and Claims from Which it Depends	**Claim 13 of Wold *et al.***	**Claim 60 of Wold *et al.***
1. A **replication-competent adenovirus vector** comprising E1A and E1B, wherein E1A and E1B are both under transcriptional control of separate a fetoprotein transcription regulatory elements (AFP-TRE). 37. A **method of suppressing tumor growth in an individual** having an AFP-expressing tumor, comprising **contacting tumor cells** with the adenovirus vector of claim 1, wherein the adenovirus vector transfects the tumor cells and replicates. 63. The method of claim 37, wherein said vector comprises a sequence encoding an ADP polypeptide.	13. A **method for treating cancer in an animal having a tumor** comprising **administering to the tumor** an **adenovirus vector wherein said adenovirus vector is replication-competent** in neoplastic cells and overexpresses an adenovirus death protein (ADP), wherein overexpression is defined as overexpression relative to *dl*309.	60. A **method for treating cancer in an animal having a tumor**, the method comprising **administering to the tumor an adenovirus vector that is replication-competent in neoplastic cells** and expresses an adenovirus death protein (ADP), wherein: ... b) the adenovirus vector comprises a deletion in the E3 region that removes a splice site for an E3 mRNA; .... 72. The method of claim 60, wherein the adenovirus vector comprises a deletion in the E3 region that removes a splice site for an E3 mRNA.

As should immediately be evident, present claims 13 and 60 are distinct from claim 63 of Little, which contains the following recitations:

- a first AFP promoter controlling the expression of E1A
- a second AFP promoter controlling the expression of E1B
- an AFP-expressing tumor

Similarly, claims claims 13 and 60 of Wold *et al.* have distinct recitations when compared to Little claim 63:

- overexpression of ADP
- E3 splice recitations

Thus, the claims cannot by definition be conflicting.

(2) Comparison of Claim 32 of Henderson with Present Claims 13 and 60

As set forth above, the Decision on Appeal did not indicate which particular claim of Henderson is alleged to claim the same subject matter as the claims of Appellants. Regarding the Henderson claims, Appellants focus on claim 32 of Henderson, as it appears to be representative of the subject matter of Henderson that would be most likely to be alleged to be identical to present claims 13 and 60. Points in common between the various claims are shown with bold type, and underlining indicates points of distinction:

Henderson Claim 32 and Claims from Which it Depends	**Wold *et al.* Claim 13**	**Wold *et al.* Claim 60**
1. A **replication-competent adenovirus vector** comprising an adenovirus gene under transcriptional control of a probasin transcriptional	13. A **method for treating cancer in an animal having a tumor** comprising **administering to the tumor** an **adenovirus vector**	60. A **method for treating cancer in an animal having a tumor**, the method comprising **administering to the tumor an adenovirus vector that is**

regulatory element (PB-TRE). 14. The **adenovirus vector** of claim 1, further comprising at least one additional adenovirus gene under transcriptional control of at least one additional prostate-specific transcriptional regulatory element. 32. A **method of suppressing tumor cell growth,** said method comprising **contacting a tumor cell** with an adenovirus vector of claim 14 **such that the adenovirus vector enters the tumor cell and exhibits selective cytotoxicity for the tumor cell.**	**wherein said adenovirus vector is replication-competent** in neoplastic cells and overexpresses an adenovirus death protein (ADP), wherein overexpression is defined as overexpression relative to *dl*309.	**replication-competent in neoplastic cells** and **expresses an adenovirus death protein (ADP),** wherein: ... b) the adenovirus vector comprises a deletion in the E3 region that removes a splice site for an E3 mRNA; .... 72. The method of claim 60, wherein the adenovirus vector comprises a deletion in the E3 region that removes a splice site for an E3 mRNA.

Again, it should immediately be evident that present claims 13 and 60 are distinct from claim 32 of Henderson, which contains the following recitations:

- PB-TRE controlling the expression of an adenovirus gene
- a second adenovirus gene under a second prostate specific promoter

Similarly, claims claims 13 and 60 of Wold *et al.* have distinct recitations when compared to Henderson claim 32:

- ADP
- overexpression of ADP
- E3 splice recitations

Thus, the claims cannot by definition be conflicting.

(3) The Little Claims Fail to Anticipate Appellants' Claims and *Vice Versa*

Independent claim 13 of the present invention recites an adenovirus vector that is replication-competent in neoplastic cells and "***overexpresses*** an adenoviral death protein" (emphasis added). The only claim in Little which makes reference to ADP is claim 63, which recites "wherein said vector comprises a sequence encoding an ADP polypeptide." However, this recitation does not set forth whether the ADP is expressed at wild-type levels, or under- or overexpressed as compared to wild-type or *dl309*. Therefore, the Little claims do not anticipate Appellants' claims.

Furthermore, present claim 72, which depends from claim 60, recites subpart (b), which pertain to a certain structural limitation of the adenovirus vector "wherein the adenovirus vector comprises a deletion in the E3 region that removes a splice site for any of the E3 mRNAs." The claims of Little fail to anticipate this feature for the simple reason that they do not recite vectors having this particular structural limitation.

By the same token, the Little claims recite vectors "comprising E1A and E1B, ***wherein E1A and E1B are both under transcriptional control of separate a fetoprotein regulator elements.***" Little claim 1 (emphasis added). Each of the Little claims depends from claim 1, and thus also include this recitation. Appellants' claims do not recite any information pertaining to the E1A and E1B genes, ***which are completely different genes from ADP***, nor do they recite any information pertaining to alpha-fetoprotein (AFP) regulatory elements. Therefore, Appellants' claims fail to anticipate the Little claims.

There also is no anticipation of the Little claims to methods of suppressing tumor growth (see, *e.g.*, claim 37) because each of these method claims recites "an individual ***having an AFP-expressing tumor***" (emphasis added). In contrast, Appellants' claims are generic on this feature,

merely reciting "an animal having a tumor." See present claims 13 and 60. Thus, the subject matter of Appellants' claims fail to anticipate the claims of Little due to the inclusion of the AFP promoter recitation in Little's claims.

(4) The Henderson Claims Fail to Anticipate Appellants' Claims and *Vice Versa*

Independent claim 13 of the present invention recites an adenovirus vector that is replication-competent in neoplastic cells and "***overexpresses*** an adenoviral death protein." (emphasis added). The only claim in Henderson which makes reference to ADP is claim 3, which recites "further comprising an adenovirus death protein gene (ADP)." However, this recitation does not include levels of ADP expression – either more or less than wild-type or *dl309*. As such, the Henderson claims fail to anticipate those of the present application.

Also, as discussed above, claim 72 recites subpart (b) pertaining to a certain structural limitation of the adenovirus vector "wherein the adenovirus vector comprises a deletion in the E3 region that removes a splice site for any of the E3 mRNAs." In contrast, the claims of Henderson fail to recite vectors that contain this structural limitation and thus cannot be anticipatory of at least this claim.

By the same token, Henderson's claims are not anticipated by Appellants' claims because Appellants' claims do not recite vectors "comprising an adenovirus gene under transcriptional control of ***a probasin transcriptional regulatory element (PB-TRE)***," as set forth in Henderson claim 1, and all other Henderson claims (emphasis added). Appellants' claims do not recite any information pertaining to a PB-TRE, and thus cannot anticipate the claims of Henderson.

(5) The Claims of Henderson and Little Do Not Render the Present Claims Obvious or *Vice Versa*

As discussed in the preceding pages, there are numerous limitations found in the claims of Henderson and Little that are not found in the present claims, and there are limitations found

in the present claims that are not found in Henderson or Little. Thus, novelty has been established. With regard to an analysis of patentable distinction, Appellants again point out that obviousness requires a teaching of each element of the claimed invention in one or more claims, optionally combined with a secondary reference. It also requires a showing that there was a motivation to combine the elements, and a likelihood of success in so doing. *In re Vaeck, supra.*

Presently, there is only one other reference cited – Freytag – from which one could possibly derive the elements clearly missing from the Henderson and Little claims. However, as noted in their Appeal Brief at page 26, Freytag cannot cure the deficiencies of the primary references (*e.g.*, overexpression of ADP or deletion of E3 splice sites), as no such teaching in Freytag can be found. Rather, Freytag has merely been cited as teaching "a novel three-pronged approach to kill cancer cells selectively comprising administration of a cytolytic replication-competent, E1B-attenuated adenovirus in conjunction with chemotherapy ... and radiotherapy." Thus, Appellants' claims cannot be deemed obvious over the claims of the primary references as there simply is no art of record to teach or suggest the affirmative claim limitations set forth above. Moreover, no discussion has been provided regarding why one of skill in the art would be motivated to combine the elements set forth in present claims 13 and 60(72), and why that person could do so with a likelihood of succeeding. These constitute additional significant deficiencies in the Board's analysis.

Furthermore, the Board failed to even discuss the ***other*** required prong of the "two-way" test, namely, whether Little and Henderson's claims were rendered obvious by Appellants' claims. Indeed, with respect to Little, none of Appellants' claims specifically addresses tumors that express AFP, and no secondary reference was cited to cure this deficiency. Similarly, Appellants' claims do not obviate the claims of Henderson as they fail to recite anything about a

probasin transcriptional regulatory element. Again, no secondary reference was cited to cure this defect. Thus, because Appellants' claims alone do not teach or suggest each limitation of the Little and Henderson claims, and no other references are cited, there can be no finding of obviousness.

(6) Conclusion

In conclusion, Appellants submit that there is insufficient evidence of record to support a finding that Appellants' claims are directed to the same subject matter of Henderson and Little. To the contrary, the evidence of record indicates that the present claims are in fact patentably distinct from those of the cited references. Thus, the Board's invocation of 37 C.F.R. §41.203(a) was not proper, and the Rule 131 declarations should have been considered.

3. Substantial Evidence Supports a Reversal of the Rejection of Claim 32 and 104-106 Under 35 U.S.C. §112, First Paragraph

The Board, in its Decision on Appeal, reversed each of the rejections under 35 U.S.C. §112, first paragraph, except for a rejection of claim 32 and claims 104-106. Claims 32 and 104-106 stand rejected as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, *i.e.*, a "written description" rejection. It is respectfully requested that the Board reconsider its Decision on Appeal, as substantial evidence weighs in favor of a conclusion that one of skill would certainly conclude from even a casual reading of the specification that the inventors' contemplated that either one or cell lysis, virus release, or cell spreading could be used to assess ADP overexpression.

a) *The Specification Specifically States that Cell Lysis is One Means of Determining ADP Over-Expression*

As set forth in Appellants' opening Brief (pages 10-11), the subject specification specifically states that cell lysis is one means of determining ADP overexpression ("...overexpression of ADP increases the rate of cell lysis"). Indeed, the entire second and third paragraph of Example 2 of the specification, page 25, demonstrates the usefulness of cell lysis to assess ADP overexpression. As set forth in those paragraphs, cell lysis assays were specifically used to *confirm* ADP overexpression in the claimed adenoviruses: "[o]nly 25% of the KD1-infected cells and 9% of the KD3-infected cells were alive at 5 days p.i. as compared to 44% of cells infected with dl01/07, which has the same E1 mutation as KD1 and KD3." Specification, page 25, lines 14-16. The specification also disclosed measuring the ***rate*** of cell lysis as a means of determining ADP overexpression: "KD1 and KD3 vectors also lysed cells faster than dl309, which has a wild-type E1A region." Specification, page 25, lines 16-17. As concluded in Example 2, "ADP is required for efficient cell lysis, and over-expression increases the rate of cell lysis." Specification, page 25, lines 20-21. Therefore, one of skill in the art is specifically apprised by the specification that cell lysis is a suitable means of assessing ADP overexpression.

Thus, in light of the preceding discussion it is submitted that substantial evidence supports the conclusion that the inventors contemplated that the cell lysis assay was one of several means for determining ADP overexpression.

b) *Virus Release Assays Were Also Employed to Assess ADP Overexpression*

A virus release assay was assessed as "***another means to measure cell lysis*** and to examine virus replication in cancer cells." Specification, page 25, lines 22-25 (emphasis added). Virus was found to be "released much more rapidly from cells infected with KD1 and KD3,

which overexpress ADP [by immunoblot], than with viruses expressing wild-type amounts of ADP." Specification, page 25, lines 28-30. One of ordinary skill in the art, in view of the disclosure, would understand that the virus release assay is another means to measure cell lysis, and also correlates with immunblot assessment of ADP overexpression. Again, these correlative studies provide substantial evidence from which the skilled artisan would conclude that the inventors contemplated that the virus release assay was one of several means for determining ADP overexpression.

c) Inhibition of Cell Spreading Correlates with ADP Expression

Cell spreading assays are yet another measure of cell lysis and ADP, as clearly indicated in FIG. 5 and the corresponding legend from the instant application. Regarding the amount of spread in cell monolayers, it was found that "the monolayer was virtually eliminated by KD1 and KD3 at 10^{-3} PFU/cell, whereas 1.0 PFU/cell was required with *dl*01/07, *dl*309 and Ad5." Page 26, lines 4-6. As explained in the first full paragraph of page 26 (lines 4-13), "[t]his result [of the cell spreading assay] ***attests to the potency of ADP in mediating cell lysis and virus spread*** in A549 cells [the target cells used in the assay]." (emphasis added). One of ordinary skill in the art, in view of the disclosure, would understand that the cell spreading assay is another means to measure cell lysis, and also correlates with immunblot assessment of ADP overexpression. Again, these correlative studies provide substantial evidence from which the skilled artisan would conclude that the inventors contemplated that the virus release assay was one of several means for determining ADP overexpression.

d) Conclusion

The Board, in affirming the rejection of claims 32 and 104-106, maintains that Appellants have made "no statement" that these assays directly correlate with ADP overexpression.

Decision on Appeal, page 8. Appellants are not required, however, to make any such statements in their disclosure. Rather, it is the evidence of record, summarized above, that demonstrates to one of skill in the art that Appellants did indeed contemplate each of the preceding assays as methods for detecting ADP overexpression. Indeed, that evidence establishes that cell lysis, cell spreading, and virus release correlate with ADP overexpression, and thus can be used to detect ADP overexpression. Accordingly, it is respectfully submitted that the Board reverse the rejection of claims 32 and 104-106.

C. CONCLUSION

WHEREFORE, Appellants respectfully request that the Board reverse the rejection of claims 32 and 104-106 under 35 U.S.C. §112, first paragraph; and the rejections under 35 U.S.C. §102(e); and the rejections under 35 U.S.C. §103(a).

Respectfully submitted

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